The Gastric Mucosa.

By

Robert K. S. Lim.

(From the Department of Physiology, Edinburgh University.)

With Plate 8 and 1 Text-figure.

Introduction

THE gastric mucous membrane is described as being disposed in three regions, known as the cardiac, fundic, and pyloric. These regions, although distinguished from one another by definite microscopic characters, yet merge gradually the one into the other, so as to present no well-defined lines of demarcation. The actual extent of each region varies in different animals. It has not been sufficiently recognized, however, that the cardiac and pyloric areas are very small, especially in the carnivora. In the cat, the (microscopic) pyloric region is a narrow zone, extending for not more than 35 mm. from the junction of pylorus and duodenum ; it may not even correspond in extent with the so-called pyloric antrum. In view of this fact it is possible to doubt the exactness with which pure pyloric pouches can be isolated either by the Heidenhain (**13**) or Pavlov (**21**) technique.

What is known regarding the functions of the different regions of the stomach is not compatible with their differences in structure. And current descriptions of the cells forming the gastric glands are by no means uniform, much confusion being due to the fact that the histological descriptions vary according to the method of fixation and staining employed and the species of animal investigated.

The following description of the histology of the gastric glands is divided into three parts. In Part I only the gastric mucosa of the cat will be described, since the observations

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I have made upon its stomach are more complete than in the other cases. Other animals, both adult and foetal, have, however, also been investigated, and the special features of some of the cells of their glands are described in Parts II and III.

PART I. THE GASTRIC MUCOSA OF THE CAT.

The cats were killed both while fasting and at various intervals after a meal. They were usually fed on boiled fish, milk, and bread, but some were put on a meat and milk diet. In all twenty-five animals have been examined.

HISTOLOGICAL TECHNIQUE.

For microscopical purposes the animals were killed either by carbon monoxide or chloroform. The stomach was then examined fresh or was prepared for sections.

For the fresh preparations a piece of the mucous membrane was either scraped off and teased in Ringer or serum, or the fresh tissue was frozen in a little serum and cut up with a microtome. The fresh sections, however, gave no more information than those obtained after fixation, so that this method was discontinued.

For permanent preparations the fixatives used were Zenker, Altmann's fluid, osmic acid 1 per cent. and formol (either neutral 20 per cent. or acid 10 per cent.). When Zenker or formol was employed the stomach was slightly distended with the fixative and suspended in the same solution for the period necessary for penetration. It was then cut into suitable pieces, which were either placed in gum or carried through in the usual way into paraffin. For some preparations pieces of fresh stomach were pinned out on a cork and immersed in the fixing reagent ; this was the chief method when using osmic acid solutions, but a few pieces were fixed in osmic without stretching.

The stains employed were alcoholic eosin and methylene blue (16), haematoxylin and eosin, van Gieson, iron haema-

toxylin (Heidenhain), Mallory (**24**), or polychrome methylene blue. It has not been thought necessary to give details of the application of the above stains ; they may be found in the references indicated. In the description which follows acid formol fixation is implied, although the observations recorded have been corroborated by other methods. Where a notable difference occurs the special fixative concerned is mentioned.

The Mucous Membrane as a Whole.

It is not intended to describe the naked-eye appearances. Suffice it to say that with a lens (Sprott Boyd (**28**)) differences may be noted between the duct orifices of the pyloric region and those of the remainder of the stomach. In the former the mucous membrane is thicker and the ducts wider, longer, and more funnel-shaped than in the latter.

The gland-tubes are simple, but may branch slightly towards their blind ends. Several gland-tubes are usually served by a common duct. Only in the part of the pyloric canal close to the duodenum do the glands become markedly racemose, but the glands adjacent to the oesophagus may also take on a racemose character.

A gastric gland-tube may be described as consisting, besides the duct, of a superficial part, which is the portion of the gland-tube immediately below the duct, and a deep part composed of the remaining portion of the gland.

The Connective Tissue.

Between the glands lies the supporting connective tissue (interglandular tissue) which contains plain muscle-fibres arranged vertically, blood-vessels, lymphatics, and nerves. In addition to these there are three kinds of cells in the tissue :

(1) **Finely Granular Branched Connective-tissue Cells.**—These stain a deep magenta with polychrome methylene blue and a purplish blue with alcoholic eosin and methylene blue. They form by far the most numerous variety and are more numerous in the stomach than in other

portions of the digestive tract. This has already been noted by Cade (**5**).

(2) Finely Granular Oxyphil Leucocytes.—These are sometimes massed together in groups : more generally they are scattered throughout the mucosa.

(3) Coarsely Granular Eosinophil Cells (Pl. 8, fig. 5, *g*). These are present in least numbers. They occur mainly near the surface, and may be found between the cells lining the duct of the gland as well as in the interglandular tissue. The eosinophil granules or globules vary considerably both in number and size, some being as much as $2-3\,\mu$ in diameter. They stain with iron haematoxylin, which does not colour the oxyphil granules of leucocytes ; they are thus not unlike the cells of Paneth of the small intestine.

All three types may be found in the interglandular tissue of other animals, e. g. dog, pig, and rabbit.

The interglandular tissue is more abundant at the cardiac and pyloric ends of the stomach than in the middle of the fundic region. Here the connective tissue is more plentiful immediately under the surface epithelium.

The mucosa rests on a thick condensation (membrane of Zeissl, stratum compactum of Oppel (Text-fig. 1, A, *sc*)) of white fibrous tissue, immediately underneath which lies the muscularis mucosae. This membrane-like condensation is of interest as it is not common to all animals, e. g. it is absent in man, pig, and rabbit, but is present in cat and rat. Further, it is non-elastic and separates the muscle-fibres within the interglandular tissue from the muscularis mucosae. It is perforated by vessels, and the plain muscle-fibres reach the mucosa by the same communications.

The Surface Epithelium.

This epithelium includes the cells covering the surface and those lining the ducts. These cells are essentially of one type. Those on the surface are columnar, becoming shorter and more cubical as they are traced into the ducts. A corresponding change may also be noted in the nucleus, which is elongated
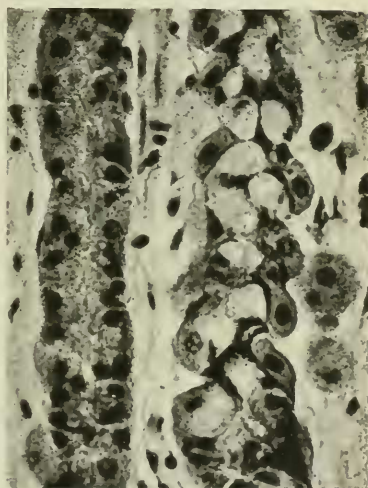
on the surface but almost spherical within the ducts (see
Pl. 8, fig. 5).

The cytoplasm is finely granular in the fresh and certain
fixed (neutral formol, osmic) specimens, and may be differen-

TEXT-FIG. 1.
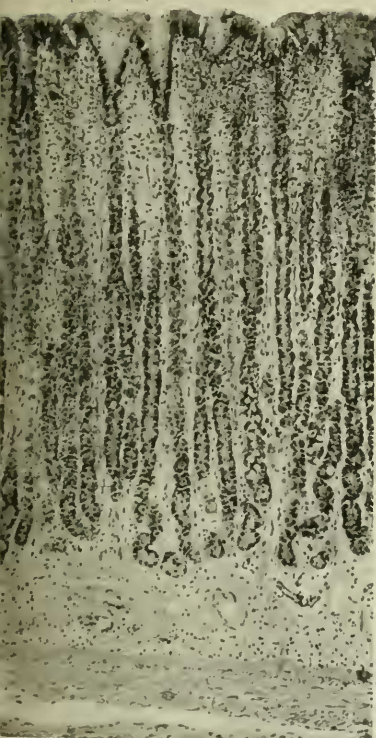
Low power (× 75).   sc, stratum com-
pactum ; mm, muscularis mucosae.

B. High power (× 400).   p, gland
lined with peptic cells ; m, gland
lined with mucoid cells ; oxyntic
cells occur in the parietal parts of
both glands.

Glands from the middle of the anterior surface of the stomach. Cat 10 ;
24 hrs. ; acid formol ; haematoxylin and eosin. (Photograph.)

tiated into two parts (Ellenberger and Scheunert (11) by
staining methods, viz. an outer goblet-shaped part, which is
clear but tinted red in haematoxylin and eosin preparations,
stained blue by Mallory and a pale blue by polychrome
methylene blue, and an inner part consisting of the remainder

of the cell, in which the nucleus is situated, and which is stained of a reddish colour by Mallory.

The surface cells show a larger goblet part than the duct-cells (see Pl. 8, figs. 3 and 5). During active digestion this part diminishes in size, but in both fasting and feeding animals cells in which the goblet part is defined but not stained may be seen. This presumably indicates that the cells in question have discharged their contents and have not had time to supply the part with new material (granules).

With regard to the mode of attachment of the cells to one another I have sometimes observed the intercellular bridges described by Carlier (5 a). These, however, are only apparent when the cells appear unduly vacuolated. In sections tangential to the surface I have seen no indications of bridges.

The surface epithelium is continuous with the epithelium of the gland-tubes, the transitional cells losing their goblet portions and staining a uniform bluish colour with Mallory. The transition is short (see Pl. 8, fig. 5, t).

The Cardiac Region.

The junction of the oesophagus and the stomach is well defined in the cat, the stratified epithelium of the former stopping abruptly and being replaced by the columnar epithelium of the latter. At this junction a lymph follicle may sometimes be seen, but there is more frequently a large vesicle or cavity lined by one or two layers of cubical cells.

The cardiac region (when present) is extremely narrow, measuring about 2–3 mm. from the cardio-oesophageal junction to the nearest group of parietal or oxyntic cells. It includes only cells of one type (cardiac cells) unmixed with others. Beyond this there is a boundary zone extending for another 3 mm., which contains both oxyntic and cardiac cells. Frequently there is no definable cardiac area ; oxyntic cells are found at the junction itself and only the ' boundary zone ' is present. Beyond the boundary zone another type of cell, characteristic of the fundus, is met with ; this may be regarded as the cardiac limit of the fundic region.

The glands of the cardiac region consist of relatively simple tubes, with short ducts and somewhat wide lumina. In most animals they are fairly numerous, in others only a few such glands are to be found near the oesophagus. They are lined by a single layer of columnar or cubical epithelium, which appears granular in the fresh condition. In sections, however, granules are absent and a fine reticulum is seen in its place. The reticulum is irregularly distributed throughout the cell, and is stained blue by alcoholic eosin and methylene blue, pale magenta by polychrome methylene blue, and blue with Mallory (Pl. 8, fig. 1). In some cases a reticulum which stains reddish with Mallory is present in addition to the above finer reticulum which stains blue. Haematoxylin hardly stains the ' blue ' reticulum at all, nor does it tint the spaces between the reticulum. In the case of the other stains just mentioned the spaces are coloured in the same way as the reticulum, but more faintly.

The nucleus is irregularly rounded or ovoid and is invariably situated towards the base of the cell. In a fasting animal the cell is more columnar and the nucleus less flattened than in an animal which has been fed. On the whole, however, there is little change to be noted in these cells.

No compound tubular glands such as have been described by Ellenberger (10), Edelmann (8), Schaffer (27), and others in various animals are present in the cat, nor are any structures resembling crypts of Lieberkühn met with ; this also applies to other regions of the cat's stomach.

The simple tubular glands of the cardiac region were first described by Schafer and Williams (26) in the kangaroo, and with their description those of the cardiac region agree. It will be shown later that the cardiac cells do not constitute a special type, but form a variety of mucoid cells, a term which is explained elsewhere.

The Pyloric Region.

The pyloric region is considerably larger than the cardiac in area, although smaller than is generally supposed. It extends

for about 15 mm. from the pyloro-duodenal junction along
the greater curvature and about 12–15 mm. along the lesser
curvature. Beyond these limits small oxyntic cells make their
appearance, and about 20 mm. further full-sized oxyntic and
peptic cells are met with in large numbers. Here lies the
pyloric limit of the fundic region.

With regard to the general features of the pyloric glands,
they have long and wide ducts and become more racemose
and exhibit more interglandular tissue near the intestine.
Lymph-follicles are numerous in this region of the stomach,
several being invariably present at the pylorus itself. At the
pyloro-duodenal junction the pyloric glands pass through the
muscularis mucosae, which is here incomplete, and become
Brunner's glands of the duodenum. The lumen of the glands
is large, and this, along with their racemose character, serves
to distinguish the pyloric glands from those of the cardia which
they otherwise resemble.

The glands of the pyloric region are lined by a single layer of
cells, which are columnar or cubical in shape and irregularly
reticulated (Pl. 8, fig. 4). They are stained in the same way
as the cardiac cell, the whole cytoplasm appearing blue with
methylene blue combinations and with Mallory, pale magenta
with polychrome methylene blue, and colourless with haema-
toxylin. As is the case with the cardiac cell, the basal portion
of the cell may in some animals be occupied by a second
reticulum which stains red with Mallory. This may be seen
in fasting and fed animals, but more often in the latter con-
dition. The nuclei are irregularly rounded and situated
basally. During activity the cell becomes shorter, indicating
a discharge of its contents, and the nucleus appears more
spherical, i. e. less compressed.

The similarity between the cardiac and pyloric glands has
been noted by many observers (Cobelli (6), Ebstein (7),
Schaffer, Stohr (29), and others). Bensley (2, 3) compares the
pyloric cells with the cells lining the ' neck ' of the fundic
gland as well as with the cardiac cells. On the other hand,
Heidenhain (13), Langley and Sewall (15), Kranenberg (23),

and all later writers believe that they are fundamentally the
same as the ' chief ' cells of the fundus. It will be shown
later that there can be no doubt regarding their difference
from the ' chief ' cells, and their resemblance to the cardiac
gland-cell is too close not to regard them as identical in
structure if not in function.

The Glands of the Fundus.

Histologically, the portion of the stomach between the
cardiac and pyloric regions just described has a uniform
structure. The glands of this intermediate area are generally
known as the glands of the fundus, though they might be more
appropriately termed the glands of the body of the stomach.
The general form and arrangement of the fundic glands have
already been noted. They are simple tubes with short ducts,
and as the glands are closely packed together there is little
interglandular tissue.

Three kinds of cell occur in the glands of this region, although
hitherto, with the exception of Bensley (1) and Cade (5),
histologists have recognized only two, namely ' central ' or
' chief ' and ' parietal ' or ' superadded ' cells.

(1) Peptic Cells.—These are usually known as ' chief '
cells ; they are quite distinct from a second type of central
cell which are intermingled with them, and are described later
as mucoid cells. Peptic cells occur throughout the lower
or deep half of the gland-tube, although it is comparatively
uncommon to find this part of the tube lined wholly by such
cells. They look somewhat columnar in shape in section, but
when isolated are polyhedral.

The cytoplasm contains granules in the fresh state (Langley
and Sewall) ; these are irregular in size. On examination in
saline, weak acids, or alcohol, the granules tend to increase
in size and become less distinct. Finally they disappear,
apparently by passing into solution. A few granules always
remain unaffected.

In fixed preparations, whether formol, Zenker, or osmic, the
granules are replaced by a coarse but regular reticulum (Pl. 8,

figs. 2 and 3, p, XXI). Nevertheless, with both formol and
osmic, a few granules may be preserved : this is especially
the case after osmic fixation (Pl. 8, fig. 3, p, XX, III).   The
regularity of the reticulum suggests that the extra-granular
cytoplasm is coagulated before the granules are dissolved out.
The reticulum may therefore be taken as a rough index of
the amount and size of the granules contained in the cell.

With regard to their reaction to various dyes, both the
reticulum and the granules become intensely stained blue with
alcoholic eosin and methylene blue, deep purplish blue with
polychrome methylene blue, and brownish violet with Mallory.
They are only lightly stained by haematoxylin, but more
strongly so by the iron haematoxylin method.   The nucleus
is irregularly ovoid or rounded ; it varies in shape and position
according to the activity of the cell.

Functional changes are easily noted in these cells.   In the
fasting condition the nucleus is found towards the base of the
cell and the cytoplasm is reticulated throughout.   After a period
of activity, i.e. during digestion, the cell gradually shrinks,
and the nucleus becomes larger and occupies a more central
position.   Teased preparations seem to show that the granules
are on the whole larger in the fresh condition, while in fixed
specimens the meshes of the reticulum are wider.   Ergasto-
plasmic fibres occur at the base of the cell, while the reticula-
tions (granules) diminish near the lumen of the gland.   In
some cases (five to six hours after a large meal) half of the cell
may be occupied by ergastoplasmic fibres.   These fibres stain
in the same way as the reticulum, although more definitely
than it (Pl. 8, fig. 3, p, III, and fig. 5, p).   Langley was the
first to demonstrate the diminution of granules during activity ;
he also stated that the cells become clearer at their bases.
Later Bensley, Zimmermann (**30**), and Theohari (**23**) showed
that the basal clear zone is occupied by ergastoplasmic fibres
(prozymogen of Macallum (**19**)).   These observations I can
confirm in the cat.   The swelling of the granules during diges-
tion appears to be a stage in the conversion of zymogen into
soluble ferment and occurs more rapidly than the formation

of new granules. Hence the diminished reticulated area, and the absence of any increase in the size of the cell, contrary to Heidenhain's observation.

(2) M u c o i d C e l l s.—This other type of central cell has somewhat finer granules, and when fixed they are replaced by a fine reticulum (perhaps a precipitate) (Pl. 8, fig. 3, *m*, xx, xxi *b*). No granules ever remain intact after fixation. In the fresh condition these granules are more rapidly dissolved by reagents than those of the peptic cells ; this, perhaps, partly explains the entire absence of granules after fixation. Mucoid cells occur mainly in the superficial half of the gland-tube, but are interspaced among the coarser reticulated peptic cells towards the deeper part, and may be found throughout the whole gland-tube. In places a portion of a gland may be lined entirely by these cells. In form they are roughly globular, but variations in shape occur according to their position and fit in the tubule (Pl. 8, fig. 5, *m*).

Their staining reactions render them distinctive. They are coloured a pale blue by alcoholic eosin and methylene blue, a pale magenta by polychrome methylene blue, and a deep blue by Mallory ; as is the case with the fasting peptic cells, they are unaffected by haematoxylin. When a definite reticulum is present it stains blue with Mallory, but in some of the cells the basal portion takes on a brownish or even reddish tinge. When there is no reticulum the precipitate-like material invariably stains blue.

The nucleus is small and compressed against the base of the cell : it is generally deeply stained. Changes during digestion consist in the cell becoming first larger and later smaller and staining less heavily with Mallory, while the nucleus appears to be a little more prominent. Mucoid cells are most marked in the boundary zones, where they are continuous with the cardiac cells on the one side and the pyloric cells on the other.

(3) O x y n t i c C e l l s.—In the cat these cells are mostly found wedged in between the central cells with a corner abutting on the lumen ; nevertheless, they lie sufficiently far outwards to be termed parietal cells. They are most numerous

in the superficial half of the gland, and may form the sole lining of a portion of the gland-tube. They may be found even between the columnar cells of the gland-ducts. In shape (judging from vertical and transverse sections) they are roughly pyramidal, but there are many variations from ovoid to crescentic. Unlike the peptic and mucoid cells the granules of the oxyntic cells are very fine, and are not readily attacked by reagents. They are fixed by all the methods employed; with osmic acid those situated immediately underneath the membrane of the cell may be demonstrated to be lipoid in character. Similar observations have been made by Böhm and Davidoff (4) in the rat. The staining reactions of the oxyntic cell-granules are as follows : red with alcoholic eosin and methylene blue, haematoxylin and eosin and Mallory ; pale blue with polychrome methylene blue ; and dark brown with osmic.

The nucleus is spherical and usually central. Occasionally it is excentric or there may be two nuclei within the same cell.

A number of the cats examined showed the presence of parasitic spirochaetes (Lim (18)). These organisms were sometimes found within oxyntic cells in what appeared to be a single dilated canaliculus, continuity with the lumen of the gland being demonstrated. Otherwise there was no histological disturbance. Vacuoles may often be seen within the oxyntic cells of all animals.

With regard to functional changes, oxyntic cells appear on the whole to become larger (Heidenhain) during digestion and their granules more easily distinguished, being less closely packed together and probably fewer in number. The difference, however, is not marked, and may be partly due to shrinkage of the central cells.

It ought to be noted that oxyntic cells occur throughout the whole stomach, being absent only some 3 mm. from the oesophagus and about 15 mm. from the pyloro-duodenal junction. The oxyntic cells of the pyloric boundary zone are somewhat small in size and are situated mainly in the superficial portion of the gland ; they are probably primitive in

character. These have already been described in other animals
(Stöhr (**29**), Trinkler (**23**), Nussbaum (**20**)). Nussbaum, how-
ever, does not consider these smaller cells to be the same as
oxyntic cells.

General Considerations.

These observations show firstly that the term ' chief ' or
' central ' cells is inadequate, since there are two types differing
widely from each other. Secondly that the cells of the cardiac
and pyloric regions are similar in structure and of the same
characteristics as the mucoid cells of the fundus. Thirdly that
the fundus is the all-important region of the stomach from
the point of view of the secretion of gastric juice, the other
two regions being small by comparison and containing no
recognizable zymogen-secreting cells.

Let us first consider the characters of the two types of central
cells. We have seen that the peptic cell is granular (or reticu-
lated) and that after a period of activity the granules diminish
in number and are replaced at the base of the cell by ergasto-
plasmic fibres. In the case of the mucoid cell the cytoplasm
is also granular (when fresh), but functional changes do not
cause any alteration in its architecture. The nucleus of the
peptic cell at rest is irregularly rounded or ovoid, and is applied
against the basement membrane, but during digestion is more
regular in outline and frees itself from the base so far as to
occupy a more central position. The mucoid cell-nucleus, on
the other hand, is not markedly changed either in shape or
position. There are also the differences in staining reactions.
The peptic cell is coloured in an entirely different manner
from that of the mucoid cell (compare m and p, Pl. 8, fig. 3).
This difference is manifested not with one staining method
alone but with several, although Mallory's is the best for the
purpose. Both types of central cell may be seen in man, dog,
and rabbit (and also in the frog) ; they are probably common to
all mammals.

There can thus be no doubt regarding the separate existence
of these two types of cells. Edinger's theory that all the

varieties of cells found in the stomach are functional modifica-
tions of one type is untenable. It is impossible to reconcile
this view with the differences in structure and reactions in
both fasting and feeding animals.

Heidenhain (**13**) long ago observed that some chief cells
stain more readily with aniline blue than others —and referred
this to functional changes. This was later confirmed by Green-
wood (**12**) in the pig's stomach ; she suggested that the ' clear '
cells might be mucus cells, thus anticipating the results of two
subsequent observers. Both Bensley and Cade have distin-
guished two types of central cells (older observers from
Edinger (**9**) and Pilliet (**22**) downwards have found various
modifications of the central cells but not separate types),
which appear to be similar to the peptic and mucoid varieties
described here. Bensley was the first to note that the cells
of the ' neck ' region of the fundic glands stain in the same
manner as mucus-secreting cells ; these cells he termed ' in-
dulinophilous mucous cells '. Cade confirmed Bensley's finding
with indulin and called them ' cellules principales du col '.
In the cat the neck region is lined by oxyntic and transitional
cells, i. e. cells which have almost lost the division of the
cytoplasm into two zones so characteristic of the surface
mucous cells (see Pl. 8, fig. 5, *t*). It is the portion of the gland
below the neck, therefore, that is lined chiefly by mucoid
cells (see Pl. 8, fig. 5). Bensley (**2**) does state, however, that
an occasional ' indulinophilous cell ' may be found among the
central (peptic) cells of the deeper part of the gland, and from
an examination of his figures (Pl. 8, fig. 6) it is clear that the
neck region he describes includes the superficial portion of the
gland. To him credit is due for their discovery, although
a more definite description and wider distribution of the mucoid
cells must now be recognized.

' Mucoid ' cells are described in only two text-books in
English, Schafer's ' Essentials of Histology ' (**25**), and the
American edition of Böhm and Davidoff, translated by Huber
(**4**). Of continental works I can only find a mention in Prenant,
Bouin, and Maillard (**23**), who have an excellent diagram in

their text-book of Histology showing typical mucoid cells—
which they hesitatingly label ' cellules principales muqueuses ? '
—to illustrate the mucus cells of Bensley.   It is evident.
therefrom, that hitherto the distribution and even the existence
of mucoid cells have scarcely been recognized.

The names ' peptic ' and ' mucoid ' have been chosen for
obvious reasons.   The structure of the peptic cell is charac-
teristically that of a zymogen-secreting cell, and by the term
' chief ' or ' central ' this cell was meant, so that there is no
need to dispute its function.   The term mucoid is applied
because the cell resembles other mucus-secreting cells, but it
is not identical either with the mucus-secreting cells lining
the surface or with the goblet cells of the intestine (compare
cells m and s in Pl. 8, fig. 3 ; also see Lim (17)).

We may next consider the relation between the cardiac,
pyloric, and mucoid cells.   We have seen that there is little
or no difference structurally between the two former (cardiac
and pyloric) cells, and that the mucoid cells resemble them in
most respects except position.   They are stained in the same
way, and their structural characters are very similar both
during rest and activity.   The cardiac and pyloric cells show
in some animals a reddish basal reticulum ; this may or may
not constitute a difference, although it is to be noted that the
reticulum is more frequently absent than present.   Lastly,
they are continuous with each other, for cardiac cells can be
traced into the fundus in the form of mucoid cells ; the same
applies to pyloric cells.   The close resemblance which thus
exists between these three types (they are all obviously mucoid)
presumes a similarity in their functions.

The striking differences in structure between the peptic
and pyloric cells have been quite missed by all the workers
on pyloric pouches, and it is possible that their histological
examination was inadequate to ensure the purity of the
pouches which they made.   But apart from this the suggestion
that pepsin is secreted by cells which are not typical of the
zymogen-secreting type calls for a closer investigation into
the origin of the secretion of the pyloric pouches.

Summary.

The gastric mucous membrane is principally formed by relatively simple tubular glands which become more complex near the orifices of the viscus, especially near the pylorus. The glands are lined by one or more kinds of cells : the following types may be recognized :

1. Surface mucus-secreting cells, which include the cells lining the surface and the gland-ducts leading therefrom.

2. Mucoid cells, of which there are two closely allied groups, viz. :

  (a) The cardiac and pyloric cells which form the sole lining of the glands within about 0–2 mm. and 15 mm. of the oesophageal orifices respectively.

  (b) The mucoid cells proper, which occur in the large intervening region (fundus) where they are intermingled with the peptic and oxyntic cells ; they chiefly occupy the superficial or upper part of the gland-tube.

3. Peptic cells, which are found (often in conjunction with mucoid cells) within the deep part of the gland ; both peptic and mucoid cells were formerly described as ' chief ' or ' central ' cells.

4. Oxyntic cells, which chiefly occupy the upper portion of the gland where they are found between the mucoid cells ; in the deeper portion of the gland they take up a parietal position.

The interglandular tissue contains basiphil connective-tissue cells, oxyphil leucocytes, and a few cells with large eosinophil globules.

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PART II. THE GASTRIC MUCOID CELLS OF FOETAL AND NEW-BORN ANIMALS.

The stomachs of two litters of new-born and of one foetal cat have been examined, and in addition those of three still-born children and one four months' human foetus. The method employed was acid formol fixation ; the staining was effected with either Mallory's stain or Heidenhain's iron haematoxylin.

CAT.

In a foetus of about six weeks the stomach exhibits a simple lining of columnar epithelium, which is entirely

devoid of a superficial mucous portion. The cytoplasm stains reddish with Mallory. Only a few invaginations represent the primitive gland-tubes.

At birth short simple gland-tubes are present. They are lined by oxyntic and mucoid cells. Some of the latter are wholly, others are only partially, mucoid, having a portion of non-mucoid (red-staining with Mallory) cytoplasm within the basal half of the cell. The surface cells are similar to those of the adult.

One week after birth the glands are larger and the oxyntic cells more prominent. Mucoid cells are present in large numbers ; a few developing peptic (?) cells are visible. These show no mucoid reaction ; they are coloured principally by the red and brown dyes in Mallory's mixture. The pylorus is now becoming defined ; it contains only mucoid cells.

Three weeks after birth the peptic, mucoid, and oxyntic cells are all plainly evident ; the appearance of the mucous membrane now approximates that of the adult.

Human.

In a foetus of about four months the stomach is lined by a mucous membrane of the simple type, bearing only short gland-tubes. These are formed partly by mucoid and partly by red-staining non-mucoid cells ; oxyntic cells are as yet absent. The junction between the stomach and the duodenum is sharply marked off by the pyloric sphincter, but the mucous membrane does not show a corresponding division. The pyloric portion of the stomach for some distance from the actual muscular junction contains both goblet and columnar cells with striated borders. The glands are wholly mucoid.

At birth peptic and oxyntic cells are fully developed : the glands are much longer than at four months and altogether more like the adult.

Conclusions.

It is quite clear that the gastric glands are in the first instance formed of non-mucoid, red-staining cells. Later these

cells become mucoid in character throughout the whole stomach. The next type to differentiate is the oxyntic, and at a later stage still comes the peptic.

Peptic cells are present in the human foetus at birth, but in the cat do not appear until between the second and third week after birth. This difference may give an important clue to the function of the fundic mucoid cells, for it has been observed that the new-born human stomach contains pepsin while the stomach of the new-born cat contains none, and does not exhibit a ferment until the third week after birth ((Hammarsten 1874, Zweifel 1874, Morrigia 1876) quoted by Moore (2), Sewall (3)). Obviously pepsin is not secreted by the mucoid cells.

These cells are essentially primitive, or at least less specialized than either the peptic or oxyntic. Cade arrives at a parallel conclusion from an entirely different point of view (1). He found that oxyntic cells disappear and peptic cells lose their granules in the vicinity of gastero-enterostomy openings, and all the cells appear mucoid in character. He thus inferred that the altered conditions had caused the specialized cells to revert to the more primitive mucoid cells. In cats I have been able to confirm Cade's observation completely.

Thus while the mucoid cells are undoubtedly a definite variety of the gastric gland-cells they are closely allied to the peptic cells to which they give rise in early and perhaps in later life.

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PART III. THE GASTRIC MUCOID CELLS IN MAN, DOG, RABBIT, AND FROG.

The gastric mucous membrane of several species of animal has been examined in order to compare the histological features and the distribution of the mucoid-reacting cells in each

species, and to determine the general relationship which exists between the mucoid group and the peptic cells of the fundus. The technique employed is similar to that referred to in Part I. The material was invariably obtained from the newly-killed or from the living anaesthetized animal. Human material came partly from the operation table, partly from the post-mortem. Acid formol fixation and Mallory's and Heidenhain's methods of staining were the routine procedures.

The Mucoid Cells of the Fundus.

Human.—In man mucoid cells are abundantly present. They have the same characteristics as those of the cat except that their cytoplasm is more homogeneous and stains a lighter blue with Mallory. Their distribution is somewhat different ; they form the entire central lining of rather less than the superficial two-thirds of the secreting tubule—hence their regular cubical outline. This portion of the tubule is thinner than the deeper portion which (with rare exceptions) contains typical peptic and oxyntic cells. A few tubules are lined throughout their whole extent by mucoid cells. There is not the same amount of intermingling between the mucoid and peptic cells as in the cat, and thus the mucoid portion of the tubule is more easily defined, especially since it is narrower than the peptic portion.

Dog.—The mucoid cells of the dog are intermediate in appearance between those of man and the cat. In some individuals the cytoplasm is almost homogeneous and stains lightly with Mallory ; in others it is more reticular and stains heavily as in the cat. This may be due to functional changes. The distribution of the cells, however, shows fewer mucoid cells in each tubule, i.e. they line less than the superficial half ; nor do the mucoid and peptic cells intermingle to any great extent. The widening of the calibre of the deep portion of the tubule occurs gradually as in the cat, but nevertheless the mucoid and peptic portions are sharply marked off from each other.

Rabbit.—The mucoid cells of the rabbit stain faintly blue with Mallory and are nearly homogeneous ; they appear like those of man. They are not easily made out since they are

hidden by the numerous overlapping oxyntic cells. This seems to be a very characteristic feature in the rabbit and accounts for the shape of the cells being very irregular. These cells occupy the superficial three-fourths of the tubule, but there is a good deal of intermingling with peptic cells. The deep portion of the tubule rarely shows mucoid cells. This is best shown in iron-haematoxylin-stained sections of the actively secreting stomach, the presence of the overlapping oxyntic cells making it difficult to examine the more centrally situated cells. In the above preparations the peptic cells alone are clearly stained on account of the marked development in them of ergastoplasmic fibres. The mucoid cells are left unstained by iron haematoxylin. The proportion of mucoid to peptic elements in each tubule varies in different parts of the fundus ; from two-thirds to four-fifths of the whole tubule may be mainly mucoid.

Frog (Rana temporaria).—In the frog's stomach only oxyntic and mucoid cells are to be seen. The latter have a clear cytoplasm which stains a faint blue with Mallory. They are found in the superficial third of the gland-tube and rarely extend to the deeper parts.

The Cardiac and Pyloric Mucoid Cells.

The cells forming the cardiac and pyloric glands are so similar in appearance and staining reactions that they may be grouped together for consideration. They differ from the mucoid cells of the fundus in their regular shape and in sometimes exhibiting a red-staining reticulum with Mallory. The extent of the cardiac and pyloric zones along the two curvatures of the stomach have been measured and are set forth below.

Animal.	Cardiac Cells.	Cardiac and Oxyntic Cells.	Pyloric Cells.	Pyloric and Oxyntic Cells.	Curvatures.
Cat	0–4 mm.	3 mm.	15 mm.	20 mm.	Greater
	0–3 mm.	3 mm.	12–15 mm.	20–5 mm.	Lesser
Dog	—	2 mm.	20 mm.	40 mm.[1]	Greater
	—	3 mm.	25 mm.	45 mm.[1]	Lesser
Rabbit	0–1 mm.	2 mm.	35 mm.	2 mm.	Greater
	0–2 mm.	2–3 mm.	40 mm.	2–3 mm.	Lesser

[1] Oxyntic cells small and primitive.

H u m a n.—The pyloric cells of man resemble those of the cat in every respect except that they are longer and stain more lightly. Sufficient material was not available from which measurements of the cardiac and pyloric regions could be made.

D o g.—There are no pure cardiac glands in the dog. Oxyntic cells may be found at the cardio-oesophageal junction along both curvatures, while peptic cells are present within 2–3 mm. of the junction. In this small zone the cells are longer but otherwise show the same features as those of the cat. Racemose glands are very constantly present ; they extend from the oesophagus into the cardia under the muscularis mucosae. Their acini are mucous with a few serous crescents here and there. They are thus not to be considered as cardiac glands, but as part of the salivary apparatus which occurs abundantly in the mucosa of the oesophagus.

The pyloric region extends for about 40 mm. along the greater curvature and 45 mm. along the lesser. The boundary zone bearing full-sized oxyntic cells and pyloric cells occupies only about 2 mm., but small (primitive) oxyntic cells may be observed especially at the neck of the glands within 20–5 mm. of the pylorus. The cells, like the cardiac group, resemble those of the cat—the red-staining reticulum being more constantly present ; this is best seen in those near the duodenum.

R a b b i t.—There are few cardiac glands corresponding to those seen in the cat. These usually occur along the lesser curvature, occupying a small zone of about 2 mm. distal to the oesophagus. Along the greater curvature and sometimes along both curvatures oxyntic cells may be found right up to the cardio-oesophageal junction. When the cardiac glands are present the cells which form them are not typical. They only show a faint mucoid reaction near the surface ; elsewhere the cytoplasm is both granular and reticular, and stains reddish with Mallory. The condition appears to be an exaggeration of the ‘red reticulum’ seen in the cat and other animals. In addition to this peculiarity glands of the racemose type are also met with under the muscularis mucosae. They extend

(along the lesser curvature) for only a very short distance (about 3 mm.). The acini are mainly serous, a few being mucous ; the cells lining the terminal ducts have granules in striae and have centrally-placed nuclei. True mucoid and peptic elements are present beyond the cardiac area described above, the former forming a boundary zone of about 3–4 mm. with the oxyntic cells before the latter are met with.

The pyloric region is somewhat larger than that of the cat, since oxyntic cells are only seen about 35–40 mm. from the duodenum (see table, p. 207). There is almost no boundary zone ; the peptic cells appearing a few millimetres beyond the oxyntic. The gland-cells are more mucoid than those of the cardia, but like these show a well-marked non-mucoid basal area.

Langley (5) described the cells of the rabbit's fundus along the greater curvature as being finely granular and similar in appearance to the pyloric cells, while the cells of the remainder of the fundus are coarsely granular. I have not been able to make out this distinction, but perhaps Langley took the superficial mucoid cells to be the only kind of central cell and failed to see the peptic (coarsely granular) cells in the deepest part of the mucous membrane.

Frog.—There are no true cardiac glands in the frog ; the peptic cells merely stop short at the end of the oesophagus while mucoid and oxyntic cells make their appearance. The pyloric region extends about 3–4 mm. from the duodenum : its gland-cells are not different from the mucoid cells of the fundus.

General Conclusions.

The results of this investigation confirm those of Bensley (1) and more especially those of Cade (2), who has examined all the species dealt with here. They show that the fundic mucoid cells vary slightly in appearance in different animals, and that their distribution in the tubule is roughly about the superficial half. From the study of new-born cats it is found that the peptic cell arises from cells of the mucoid type. This

is also probably true for animals other than the cat, since the peptic cells are invariably found in the deep or blind end of the tubule, which may be considered to have developed last. This encourages the view that the mucoid cell gives rise to the peptic cell, without suggesting that the latter is merely a functional phase of the former. Mucoid and peptic cells are undoubtedly different functionally and structurally. In this connexion it is noteworthy that mitoses have never been observed in peptic cells, while they have been seen in mucoid and more frequently in oxyntic cells. In short the mucoid cell is a stage in the genesis of the peptic cell. Transitions from the one state to the other are difficult to demonstrate, but considering the differences, slight though they may be, which occur in the mucoid cells of the same and of different animals, and especially the occurrence of the basal ' red-staining ', the gap in the genesis of the peptic cell is perhaps partially filled. Looked at in this light, the observation of Cade on the retrogression of the peptic cells in the vicinity of gastero-enterostomy openings (see Cade (2) and Part II of this paper) may be translated as the inhibition of peptic cell-formation and the arrest of its genesis in the mucoid stage.

Utilizing the above hypothesis, the cells of the cardiac and pyloric glands may be regarded as cells which have been prevented from attaining full development by the conditions existing at the orifices of the stomach.

The relationship between the various gastric cells may therefore be classified as follows. The mucoid cell of the fundus forms the lowest functional type, for it apparently does not secrete pepsin. The cardiac and pyloric cells are a little more advanced, since Klemensiewicz (4) and Heidenhain (3) have shown that the pyloric region secretes a proteolytic ferment. Structurally these cells show the basal ' red-staining ' more constantly (especially in the rabbit) than the mucoid cell, and this may be taken as indicating a certain degree of zymogen formation. The cardiac cells may not function exactly as the pyloric cells do, but they are at least cells of the same developmental order, and they constitute such a small element in the

animals under consideration that they probably have no
physiological significance. The peptic and oxyntic cells are
the most highly specialized.

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EXPLANATION OF PLATE 8.

(All are from the cat.)

Fig. 1.—A cross section of a gland-tube from the cardiac end of the
stomach along the lesser curvature, about 1 mm. from the oesophagus.
Animal killed fourteen hours after last meal. Acid formol fixation;
stained with Mallory.

Fig. 2.—A cross section of a gland-tube from the cardiac end of the
stomach along the lesser curvature, about 6 mm. from the oesophagus.
From the same preparation as fig. 1. *m*, mucoid; *p*, peptic; *o*, oxyntic.
These cells are in the resting condition.

Fig. 3.—Cells from the glands of the middle region of the stomach.
s, surface mucus-secreting cells; *m*, *p*, as in fig. 2.

xx, Cat 20; 14 hrs.; Altmann's fluid; Mallory. The peptic cell on
the left is somewhat homogeneous (granules intact), while the cell on the
right shows the more usual reticulated appearance. Note the cytoplasm
of the mucoid cell.

I, Cat 1; 1 hr.; acid formol; alcoholic eosin and methylene blue.
The granules in the peptic cell are imperfectly preserved; the cytoplasm
stains intensely in a blotchy manner. Note the almost homogeneous
appearance of the mucoid cell.

III, Cat 3; 6 hrs.; acid formol; very dilute polychrome methylene blue.
The peptic cell here shows well-marked ergastoplasmic fibres and zymogen
granules, and is in striking contrast with the mucoid cell.

xxi *a*, Cat 21; 24 hrs.; acid formol; iron haematoxylin.

XXI *b.* same tissue ; Mallory. The peptic cells show a well-marked reticulated appearance. Note that the mucoid cells also show a reticulum.

Fig. 4.—Cross section of a pyloric gland from the lesser curvature about 19 mm. from the pyloro-duodenal junction. Cat. 21 ; 24 hrs. ; acid formol ; iron haematoxylin. The sparse reticulum which can be seen here stains red with Mallory.

Fig. 5.—A longitudinal section of a gland-tube from about the middle of the greater curvature. Cat 3 ; 6 hrs. ; acid formol ; Mallory. *s, m, p, o,* as in figs. 2 and 3 ; *t,* transitional cells ; *g,* cell containing large eosinophil globules. This drawing gives an idea of the distribution of the various cells which compose a gastric gland-tube in the fundic region. The cells are in an exhausted condition. Compare the mucoid cells with the peptic, and also this figure with fig. 2.